REMARKS

Reconsideration and withdrawal of the objections to and the rejections of this application are respectfully requested.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-18 are pending in this application. Claims 1, 9 and 14-16 have been amended; Claims 2-3, 5, 6, 10-12 and 18 have been cancelled; Claims 4, 13 and 17 have been withdrawn. No new matter is added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. §112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

II. REJECTIONS UNDER 35 U.S.C. § 112, 1ST PARAGRAPH ARE OVERCOME

Claims 9-12 and 14 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a tolerance attenuating dose of an NMDA receptor antagonist, does not reasonably provide enablement for a preventing dose of an NMDA receptor antagonist. The rejection is respectfully traversed.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988), determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors, for example, (1) the quantity of

experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. Undue experimentation is not required in this case.

As currently amended, Claim 9 does not recite a limitation to a tolerance preventing dose of an NMDA receptor antagonist. As pointed out by the Examiner, Claim 9 is enabled for a tolerance attenuating dose of an NMDA receptor antagonist, and as amended Claim 9 only recited this tolerance limitation. Claims 10-12 are canceled, without prejudice, without admission, without surrender of subject matter, and without any intention of creating estoppel as to equivalents. To the extent that Claim 14, dependent on Claim 9, has been rejected as reciting a tolerance preventing dose of an NMDA receptor antagonist, this rejection is overcome by the amendment to Claim 9.

In view of the amendments and arguments, reconsideration and withdrawal of the Section 112, first paragraph, rejections are respectfully requested.

III. REJECTIONS UNDER 35 U.S.C. § 112, 2ND PARAGRAPH ARE OVERCOME

Claims 1-3, 5-8, 11-12 and 14 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The rejection is respectfully traversed.

(i) The Examiner's rejection of Claims 1 and 11 as being vague and indefinite for including the term "derivative" has been overcome. The Examiner should take note that neither the original or currently amended Claim 1 includes the term "derivative," and therefore Claim 1 overcomes this rejection. Claim 11 has been canceled, without prejudice, without admission,

without surrender of subject matter, and without any intention of creating estoppel as to equivalents.

(ii) Claims 6 and 10 have been canceled, without prejudice, without admission, without surrender of subject matter, and without any intention of creating estoppel as to equivalents.

(iii) The Examiner has rejected Claim 14 as being vague and indefinite, as it is not clear what percent weight of an NMDA receptor antagonist is being claimed. As currently amended, Claim 14 provides for the administration of ketamine in a dose of about 0.1 % to about 5%, by weight, of total weight of ketamine and morphine. The amendment to Claim 14 makes clear what percent weight of ketamine is being claimed.

In view of the amendments and arguments, reconsideration and withdrawal of the Section 112, second paragraph rejections are respectfully requested.

IV. REJECTIONS UNDER 35 U.S.C. § 102(b) ARE OVERCOME

Claims 1-3, 6, 9-12 and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Gervitz *et al.* (5,635,204). This rejection is respectfully traversed.

Gervitz *et al.* involves a method of inducing surgical anesthesia in a mamal by transdermally administering via a transdermal patch an amount of an amnesia producing drug (ketamine), and after an amnesic state is produced, transdermally administering amounts of clonidine and fentanyl which are sufficient to produce surgical anesthesia. The method of inducing surgical anesthesia taught by Gervitz *et al.* necessarily results in the amnesia inducing use of ketamine, whereby ketamine attains "plasma level concentrations of 100-150 ng/ml", and the method of Gervitz *et al.* necessarily involves systemic or central administration. (5,635,204, Col. 2, Ln. 66-67).

Claims 1, 9 and 15 provide a topical pharmaceutical composition comprising ketamine and morphine, and methods for peripheral analgesia using the topical pharmaceutical composition. Simply, in contrast to the instant invention, Gervitz *et al.* provides "transdermal administration" that is "a general anesthetic" which results in "profound sedation." In the present claim recitations: Claim 1 recites that delivery is "not to central opiate receptors," Claim 9 recites that the method is "not central systemic analgesia ... and not centrally or systemically, analgesic dose," and Claim 16 recites "a tolerance attenuating, peripherally but not centrally or systemically analgesic dose." Gervitz *et al.* is clearly contrary to, and teaches away from, and fails to teach or suggest, the recitations of the instant claims.

The method of Gervitz *et al.* is not a single prior art reference that discloses each and every element of the presently claimed invention. The method of the present invention provides for peripheral analgesia, not systemic or central, and is therefore not previously taught or suggested by Gervitz *et al.* Accordingly, Gervitz *et al.* fails to teach the instant invention and reconsideration and withdrawal of the Section 102(b) rejections are respectfully requested.

V. REJECTIONS UNDER 35 U.S.C. § 103 ARE OVERCOME

Initially, as to all of the Section 103 rejections, reference is made to the forgoing distinctions between Gervitz *et al.* and the instant invention. Claims 5 and 14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gervitz *et al.* as applied to claims 1-3, 6, 9-12 and 15 under 35 U.S.C. 102(b) above, and further in view of Nelson *et al.* (5,840,731) and Needham *et al.* (6,261,582). The rejection is respectfully traversed.

The Examiner is respectfully reminded of the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989);

In re Obukowitz, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Gervitz *et al.* in view of Nelson *et al.* and Needham *et al.*, does not teach or suggest the present inventive concept. Claim 14 provides for peripheral analgesia that is not suggested by Gervitz *et al.* in view of Nelson *et al.* and Needham *et al.*

Further, the Office Action has failed to make a *prima facie* case for obviousness because one of ordinary skill in the art at the time of invention would not have combined Gervitz *et al.*, Nelson *et al.* and Needham *et al.* to obtain a method for providing peripheral analgesia, especially as Gervitz *et al.* teaches away from peripheral analgesia as recited in the instant claims (note the pregoing discussion as to the Section 102(b) rejection). There is no indication in the cited documents that would lead one to appreciate peripheral analgesia, e.g. with tolerance attenuation as in the instant claims.

Claims 7-8 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gervitz *et al.* as applied to claims 1-3, 6, 9-12 and 15 under 35 U.S.C. 102(b) above, and further in view of Kaneko et al. (Anethesiology '94). The rejection is respectfully traversed.

Gervitz *et al* in view of Kaneko *et al.* does not teach or suggest the present inventive concept. Claims 7-8 are directed to a pharmaceutical composition providing for peripheral analgesia, further comprising a local anesthetic. Gervitz *et al.* in view of Kaneko *et al.* does not

teach or suggest compositions providing peripheral analgesia and further comprising a local anesthetic.

Further, the Office Action has failed to make a *prima facie* case for obviousness because one of ordinary skill in the art at the time of invention would not have combined Gervitz *et al.* and Kaneko *et al* to obtain compositions providing peripheral analgesia and further comprising a local anesthetic. Moreover, there is no suggestion to combine the Gervitz *et al.* and Kaneko *et al.* documents to obtain the compositions of Claims 7 and 8. Kaneko *et al.* merely involves the coadministration of morphine and lidocaine producing analgesia, but the document does not offer any teachings or suggestions as to a pharmaceutical composition containing ketamine that provides analgesia. And as discussed above, this is also a deficiency of Gervitz *et al.*

Claim 16 was rejected under 35 U.S.C. 103(a) as being unpatentable over Gervitz *et al.* in view of Smith *et al.* (6,194,000). The rejection is respectfully traversed.

Gervitz *et al.* in view of Smith *et al.* does not teach or suggest the present inventive concept. Claim 16 is directed to a pharmaceutical tolerance attenuating analgesic kit comprising: a topical or systemic pharmaceutical composition comprising morphine that functions through an opiate receptor; and a topical pharmaceutical composition comprising a tolerance-attenuating, peripherally but not centrally or systemically analgesic dose, of ketamine. While the Smith *et al.* involves analgesic compositions comprising an NMDA receptor antagonist, including kits in a plurality of dosage forms, there is no teaching or suggestion as to peripheral analgesia, with tolerance attenuation; and Gervitz *et al.*, as discussed above, is contrary to the present claim recitations.

The Office Action has failed to make out a *prima facie* case of obviousness as to Claim 16 over Gervitz *et al.* in view of Smith *et al.*, in that the combined teachings of the documents

does not teach or suggest a topical pharmaceutical composition comprising a tolerance-attenuating, peripherally but not centrally or systemically analgesic dose, of ketamine. Gervitz *et al.* does not involve the compositions and methods of the present invention in that the present invention provides for peripheral analgesia. Gervitz *et al.* does not involve the tolerance attenuating aspect of the present invention. The same two points apply equally to Smith *et al.* And while Smith *et al.* may involve analgesic compositions comprising an NMDA receptor antagonist, including kits in a plurality of dosage forms, there is no teaching or suggestion as to peripheral analgesia, with tolerance attenuation. Further, there is no teaching or suggestion in the Smith *et al.* or Gervitz *et. al.* to combine their teachings in any way to arrive at the present invention.

Reconsideration and withdrawal of the Section 103(a) rejections are respectfully requested.

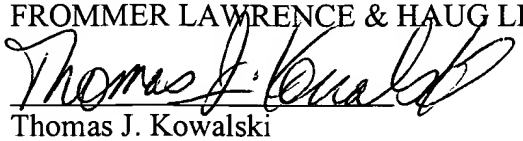
REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, an interview, with supervisory review, e.g., with the Examiner, the Primary Examiner, and the Examiner's SPE and/or a Practice Specialist, is respectfully requested prior to issuance of any paper other than a Notice of Allowance. The Examiner is additionally respectfully requested to telephonically contact the undersigned to arrange a mutually convenient time and manner for the interview. The Examiner is also invited to telephonically contact the undersigned if there are any minor, formal issues that need resolving prior to issuance of a Notice of Allowance, with a view towards resolving such minor, formal issues via telephonic interview.

CONCLUSION

In view of the amendments and remarks herewith, the application is in condition for allowance. Favorable reconsideration of the application, reconsideration, and withdrawal of the objections and rejections, and prompt issuance of a Notice of Allowance are respectfully requested.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: 

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